

CLAIMS

1. A method of protecting a human subject from progression from a normoinsulinemic state to a  
5 hyperinsulinemic state, or from either to a type II diabetic state, which comprises administering to the subject a protective amount of an agent which is

10 (1) a polypeptide which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master table 1, subtables 1A and 1C,

15 or

(2) an expression vector encoding the polypeptide of (1) above and expressible in a human cell, under conditions conducive to expression of the polypeptide of (1);

20 where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

25 2. A method of protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state which comprises administering to the subject a protective amount of an agent which is

30 (1) an antagonist of a polypeptide, occurring in said subject, which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and  
35 human proteins set forth in master table 1, subtable 1B and 1C, or

(2) an anti-sense vector which inhibits expression of said polypeptide in said subject,

where said agent protects said subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state.

5           3. A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of a  
10   "favorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is selected from the group consisting of mouse and human proteins set forth in master  
15   table 1, subtables 1A and 1C,

and directly correlating the level of expression of said marker gene with the propensity to progression in said patient.

20           4. A method of screening for human subjects who have a propensity for progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body  
25   fluid samples from said subjects to determine the level of expression of an "unfavorable" human marker gene, said human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to a reference protein which is  
30   selected from the group consisting of mouse and human proteins set forth in master table 1, subtable 1B and 1C, and inversely correlating the level of expression of said marker gene with the propensity to progression in said patient.

35           5. The method of claims 1 or 3 in which the reference protein is of subtable 1A.

6. The method of claims 1 or 3 in which the reference

protein is of subtable 1B.

7. The method of claim 3 or 4 in which the sample is a muscle tissue sample.

8. The method of any one of claims 1-7 in which the reference protein is a human protein.

9. The method of any one of claims 1-7 in which the reference protein is a mouse protein.

10. The method of any one of claims 3 or 4 in which the level of expression of the marker protein is ascertained by measuring the level of the corresponding messenger RNA.

11. The method of any one of claims 3 or 4 in which the level of expression is ascertained by measuring the level of a protein encoded by said marker gene.

12. The method of any one of claims 1-9 in which said polypeptide is at least 80% identical or at least highly conservatively identical to said reference protein.

13. The method of any one of claims 1-10 in which said polypeptide is at least 90% identical to said reference protein.

14. The method of any one of claims 1-11 in which said polypeptide is identical to said reference protein.

15. The method of any one of claims 1-14 in which the E-value cited for the reference protein in Master Table 1 is not more than  $e^{-6}$ .

16. The method of claim 15 in which the E-value cited for the reference protein in Master Table 1 is less than  $e^{-10}$ .

17. The method of claim 17 in which the E value calculated by BLASTN or BLASTX would be less than  $e^{-15}$ , more preferably less than  $e^{-20}$ , still more preferably less than  $e^{-40}$ , even

292

more preferably less than e-60, considerably more preferably less than e-80, and most preferably less than e-100.

18. The method of any of claims 2-17 in which the antagonist is an antibody, or an antigen-specific binding fragment of an antibody.

19. The method of any of claims 2-17 in which the antagonist is a peptide, peptoid, nucleic acid, or peptide nucleic acid oligomer.

20. The method of any of claims 2-17 in which the antagonist is an organic molecule with a molecular weight of less than 500 daltons.

21. The method of claim 20 in which said organic molecule is identifiable as a molecule which binds said polypeptide by screening a combinatorial library.

22. The method of claim 1 or 2 in which the agent is delivered systemically.

23. The method of claim 1 or 2 in which the agent is selectively delivered to muscle tissue.